REMARKS

The Claims

Claims 21-31 are pending in the application. Claim 21 is presently amended to clarify and more distinctly claim the invention. Such amendments place the claims in better condition for allowance or appeal and do not introduce new matter or raise new issues requiring further consideration and/or search. Entry of the amendments is respectfully requested.

Rejection under 35 U.S.C. 102

Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by WO97/23614 (Boyle et al.). The Examiner maintains that the term "having" in Claim 21 encompasses OPG with additional amino acid residues, such as amino acids 22-401 of SEQ ID NO:2 and is therefore anticipated by WO97/23614.

Without acquiescing to the rejection and solely to advance prosecution, Applicants have amended Claim 21 to recite an OPG variant or fragment selected from a deletion of one or more amino acids from positions 186-401 as shown in Figure 2 (SEQ ID NO:2) or a truncation of an amino acid sequence from positions 22-X as shown in Figure 2 (SEQ ID NO:2) wherein X is any residue from position 185 to 293 inclusive. It is believed that the rejection may be withdrawn.

Rejection under 35 U.S.C. 103

Claims 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO97/23614 (Boyle et al., hereafter "Boyle") as applied to Claim 21 and further in view of WO98/28427 (Mann et al. hereafter "Mann") Both articles were cited by Applicants. The Examiner argues that one skilled in the art would have been motivated to make the claimed OPG fusion proteins and would have had a reasonable expectation of success in doing so. Applicants disagree.

The results obtained with the claimed Fc-OPG fusion proteins are unexpected as one skilled in the art could not have anticipated that addition of an Fc region to the amino terminus of an OPG polypeptide

variant or fragment would enhance OPG activity of increasing bone density. By way of example, Table 3 demonstrates that the Fc-OPG fusion polypeptide met-FcdC-OPG[22-194] has greater *in vivo* activity than that of met OPG[22-194], the corresponding unfused OPG polypeptide fragment, which is shown in Table 2. It was unexpected that such a result could have been obtained by constructing an Fc fusion to the amino terminal end of an OPG polypeptide variant or fragment.

The Examiner argues that Boyle teaches Fc-OPG[22-401], that is, a fusion of Fc to the amino-terminus of full-length OPG[22-401] and that Boyle teaches truncated OPG polypeptides and therefore it would be obvious to make Fc-OPG or truncated versions thereof. Assuming for the sake of argument that it would have been obvious to make Fc-OPG and truncated versions thereof, Applicants point out that Fc-OPG[22-401] is not being claimed in the present application and fusions of Fc to the amino-terminus of an OPG variant or fragment gives surprising results which render them nonobvious.

The Examiner continues to allege that the disclosure of Fc-OPG[22-401] together with the conjugation of a polyethylene glycol (hereafter "PEG") molecule to the amino terminus of OPG supports the position that proteins can be added to the N-terminus of OPG and not alter activity. However, Applicants have shown that the fusion of an Fc polypeptide to the amino terminus of an OPG variant or fragment results in increased activity compared to the OPG variant or fragment itself, rather than simply maintaining the activity. It is this surprising and unexpected observation that renders the claimed OPG fusion polypeptides nonobvious. In view of these remarks, the rejection should be withdrawn.

CONCLUSION

Claims 21-31 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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